

FILE 'HCAPLUS' ENTERED AT 17:03:40 ON 22 AUG 2008
L1 23134 S ANTIDEPRESSANT
L2 11258 S ANTIPSYCHOTIC
L3 89489 S DEPRESSION
L4 123823 S (TREATMENT RESISTANT) OR REFRACTORY
L5 396 S L1 AND L2 AND L3
L6 354 S L5 NOT L4
L7 158 S L6 AND (PY<2003 OR AY<2003 OR PRY<2003)

FILE 'HCAPLUS' ENTERED AT 17:10:59 ON 22 AUG 2008
L8 44494 S BIPOLAR OR MANIC
L9 134 S L7 NOT L8

FILE 'HCAPLUS' ENTERED AT 17:12:12 ON 22 AUG 2008
L10 0 S PSYCHOSIS OR PSYCHOTIC
L11 9043 S PSYCHOSIS OR PSYCHOTIC
L12 72 S L9 NOT L11

FILE 'HCAPLUS' ENTERED AT 09:35:42 ON 25 AUG 2008

| | | | |
|----|-------|---|--|
| L1 | 23140 | S | ANTIDEPRESSANT |
| L2 | 11265 | S | ANTIPSYCHOTIC |
| L3 | 7101 | S | SUICIDE |
| L4 | 79 | S | L2 AND L2 AND L3 |
| L5 | 5875 | S | MDD OR (MAJOR DEPRESSIVE DISORDER) OR UNIPOLAR |
| L6 | 9 | S | L4 AND L5 |

| | | |
|----------------------|------------|---------|
| => file hcaplus | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'HCAPLUS' ENTERED AT 17:03:40 ON 22 AUG 2008
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FILE COVERS 1907 - 22 Aug 2008 VOL 149 ISS 9
 FILE LAST UPDATED: 21 Aug 2008 (20080821/ED)

HCAPlus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s antidepressant
L1      23134 ANTIDEPRESSANT

=> s antipsychotic
L2      11258 ANTIPSYCHOTIC

=> s depression
L3      89489 DEPRESSION

=> s (treatment resistant) or refractory
      2477638 TREATMENT
      648921 RESISTANT
      847 TREATMENT RESISTANT
        (TREATMENT(W)RESISTANT)
      123088 REFRACTORY
L4      123823 (TREATMENT RESISTANT) OR REFRACTORY

=> s l1 and l2 and l3
L5      396 L1 AND L2 AND L3

=> s l5 not l4
L6      354 L5 NOT L4

=> s l6 and (PY<2003 or AY<2003 or PRY<2003)
      22958815 PY<2003
      4496130 AY<2003
      3964380 PRY<2003
L7      158 L6 AND (PY<2003 OR AY<2003 OR PRY<2003)
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```
=> file stnguide
COST IN U.S. DOLLARS                SINCE FILE      TOTAL
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FULL ESTIMATED COST                5.38          5.59
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FILE 'STNGUIDE' ENTERED AT 17:04:53 ON 22 AUG 2008
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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Aug 8, 2008 (20080808/UP).

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=> file hcaplus
COST IN U.S. DOLLARS                SINCE FILE      TOTAL
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FULL ESTIMATED COST                0.60          6.19
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FILE 'HCAPLUS' ENTERED AT 17:10:59 ON 22 AUG 2008
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FILE COVERS 1907 - 22 Aug 2008 VOL 149 ISS 9
 FILE LAST UPDATED: 21 Aug 2008 (20080821/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s bipolar or manic
      43290 BIPOLAR
      2660 MANIC
L8      44494 BIPOLAR OR MANIC
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```
=> s 17 not 18
L9      134 L7 NOT L8
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=> file hcaplus
COST IN U.S. DOLLARS                SINCE FILE      TOTAL
                                      ENTRY      SESSION
FULL ESTIMATED COST                2.69          8.88
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FILE 'HCAPLUS' ENTERED AT 17:11:14 ON 22 AUG 2008
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FILE COVERS 1907 - 22 Aug 2008 VOL 149 ISS 9

FILE LAST UPDATED: 21 Aug 2008 (20080821/ED)

HCAPLUS now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 19 1-20 ti

- L9 ANSWER 1 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders
- L9 ANSWER 2 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of fused heterocyclic isoxazoline derivatives as anti-depressants
- L9 ANSWER 3 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of piperazinylalkylchromenoisoxazolines as antidepressants.
- L9 ANSWER 4 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of indolylalkylidenehydrazine-carboximidamide derivatives as 5-hydroxytryptamine-6 ligands
- L9 ANSWER 5 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of novel tetracyclic arylsulfonyl indoles having serotonin receptor affinity
- L9 ANSWER 6 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of tetracyclic arylalkyl indoles having serotonin receptor affinity
- L9 ANSWER 7 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of novel tetracyclic arylcarbonyl indoles having serotonin receptor affinity
- L9 ANSWER 8 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Possible role of the endogenous opioid system in the placebo response in depression
- L9 ANSWER 9 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of 7-arylsulfonamido-2,3,4,5-tetrahydro-1H-benzo[d]azepines with 5-HT6 receptor affinity for the treatment of CNS disorders
- L9 ANSWER 10 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation of 1-[2-dimethylamino-1-(4-methoxyphenyl)ethyl]-1-silacycloalkan-1-ols as therapeutic agents
 L9 ANSWER 11 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Pharmaceutical natural products containing isoflavones and hot-, sour-, and bitter-taste substances as antidepressants and antipsychotics
 L9 ANSWER 12 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of 3-arylsulfonyl-7-piperazinyl- indoles, -benzofurans and -benzothiofenenes with 5-HT6 receptor affinity for treating CNS disorders
 L9 ANSWER 13 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI An open study of olanzapine and fluoxetine for psychotic major depressive disorder: Interim analyses
 L9 ANSWER 14 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of piperazinyl-isatins useful as selective dopamine autoreceptor agonists
 L9 ANSWER 15 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Antipsychotic, antidepressant, anxiolytic, and anticonvulsant drugs induce type II nitric oxide synthase mRNA in rat brain
 L9 ANSWER 16 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI New Pyridobenzodiazepine Derivatives: Modifications of the Basic Side Chain Differentially Modulate Binding to Dopamine (D4.2, D2L) and Serotonin (5-HT2A) Receptors
 L9 ANSWER 17 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Transgenic or recombinant nonhuman mammals and their applications in screening medicaments used in psychoactive disorders
 L9 ANSWER 18 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Management of symptoms associated with advanced cancer: olanzapine and mirtazapine
 L9 ANSWER 19 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI An open pilot study combining risperidone and a selective serotonin reuptake inhibitor as initial antidepressant therapy
 L9 ANSWER 20 OF 134 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Focus on amisulpride

| | | |
|----------------------|------------|---------|
| => file stnguide | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 9.89 | 18.77 |

FILE 'STNGUIDE' ENTERED AT 17:11:30 ON 22 AUG 2008
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FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Aug 8, 2008 (20080808/UP).

| | | |
|----------------------|------------|---------|
| => file hcaplus | | |
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 0.06 | 18.83 |

FILE 'HCAPLUS' ENTERED AT 17:12:12 ON 22 AUG 2008
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FILE COVERS 1907 - 22 Aug 2008 VOL 149 ISS 9
FILE LAST UPDATED: 21 Aug 2008 (20080821/ED)

HCAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

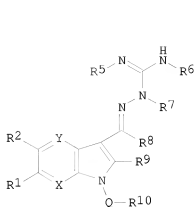
```
=> s psychosisor psychotic
      0 PSYCHOSISOR
      3146 PSYCHOTIC
L10      0 PSYCHOSISOR PSYCHOTIC
          (PSYCHOSISOR(W)PSYCHOTIC)

=> s psychosis or psychotic
      7105 PSYCHOSIS
      3146 PSYCHOTIC
L11      9043 PSYCHOSIS OR PSYCHOTIC

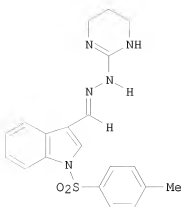
=> s l19 not l11
L12      72 L9 NOT L11

=> d l12 1-20 ti abs bib

L12 ANSWER 1 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Preparation of indolylalkylidenehydrazine-carboximidamide derivatives as
5-hydroxytryptamine-6 ligands
GI
```



I



II

AB The title compds. [I; X = N, CR3; Y = N, CR4; Q = SO2, CO, CO2, CONR11, CSNR12; R1-R4 = H, halo, CN, etc.; R5-R7 = H, alkyl, aryl, etc.; R8 = H, alkyl, cycloalkyl; R9 = H, halo, CN, etc.; R10 = alkyl, aryl, heteroaryl, 8-13 membered bicyclic or tricyclic ring; R11, R12 = H, alkyl, aryl, heteroaryl], useful for the therapeutic treatment of a disorder relating to or affected by the 5-HT6 receptor, were prepared Thus, reacting 1-[(4-methylphenyl)sulfonyl]indole-3-carboxaldehyde with 2-hydrazine-1,4,5,6-tetrahydropyrimidine.HBr in the presence of concentrate HCl in iso-PrOH afforded 42% II which showed 56% inhibition of 5-HT6 binding at 1000 nM. Pharmaceutical composition comprising the compound I is claimed.

AN 2004:3669 HCAPLUS <<LOGINID::20080822>>

DN 140:77025

TI Preparation of indolylalkylidenehydrazine-carboximidamide derivatives as 5-hydroxytryptamine-6 ligands

IN Cole, Derek Cecil; Kelly, Michael Gerard; Nunn, David Scott; Greenblatt, Lynne Padilla

PA Wyeth, John, and Brother Ltd., USA

SO U.S. Pat. Appl. Publ., 28 pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------|------------------|--|----------|-----------------|--------------|
| PI | US 20040002527 | A1 | 20040101 | US 2003-434954 | 20030509 <-- |
| | US 6906095 | B2 | 20050614 | | |
| PRAI | US 2002-379479P | P | 20020510 | <-- | |
| OS | MARPAT 140:77025 | | | | |
| RE.CNT | 8 | THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD | | | |
| | | ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | |

L12 ANSWER 2 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

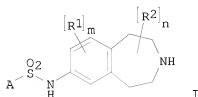
TI Possible role of the endogenous opioid system in the placebo response in depression

AB A review. The endogenous opioid system is possibly involved in placebo responses observed with pain, addictive withdrawal and treatment of depression. For this reason, psychotropic analgesic nitrous oxide (PAN) has been used for treating post-detoxification alc. depression with some success, particularly during the latent period following the initiation of antidepressant therapy. PAN has an extremely rapid onset of antidepressant action, within an hour of administration.

AN 2003:740558 HCAPLUS <<LOGINID::20080822>>

DN 140:209653
 TI Possible role of the endogenous opioid system in the placebo response in depression
 AU Gillman, M. A.
 CS South African Brain Research Institute, Johannesburg, 2090, S. Afr.
 SO International Journal of Neuropsychopharmacology (2002), 5(1), 107-108
 CODEN: IJNUFB; ISSN: 1461-1457
 PB Cambridge University Press
 DT Journal; General Review
 LA English
 RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of 7-arylsulfonamido-2,3,4,5-tetrahydro-1H-benzo[d]azepines with 5-HT6 receptor affinity for the treatment of CNS disorders
 GI



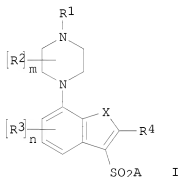
AB The title compds. [I; R1 = H, halo, OH, etc.; R2 = H, alkyl; m = 1-3; n = 1-4; A = (un)substituted Ph, naphthyl, monocyclic or bicyclic heteroaryl] and their pharmaceutically acceptable salts, useful in the treatment of CNS and other disorders such as depression, anxiety, Alzheimer's disease, age related cognitive decline, ADHD, obesity, mild cognitive impairment and schizophrenia, were prepared E.g., a 4-step synthesis of I.HCl [R1, R2 = H; A = 3-F3CC6H4], starting from 7-nitro-2,3,4,5-tetrahydro-1H-benzo[d]azepine, was given. The exemplified compds. I were tested and showed good affinity for the 5-HT6 receptor, having pKi values > 8 at human cloned 5-HT6 receptors. Pharmaceutical composition comprising the title compound I was claimed.

AN 2003:656750 HCAPLUS <<LOGINID:20080822>>
 DN 139:197390
 TI Preparation of 7-arylsulfonamido-2,3,4,5-tetrahydro-1H-benzo[d]azepines with 5-HT6 receptor affinity for the treatment of CNS disorders
 IN Bromidge, Steven Mark; Johnson, Christopher Norbert; Moss, Stephen Frederick; Rahman, Shahzad Sharooq; Witty, David R.
 PA Glaxo Group Limited, UK
 SO PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|--------------|
| WO 2003068751 | A1 | 20030821 | WO 2003-EP1543 | 20030213 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, | | | | |

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003206909 A1 20030904 AU 2003-206909 20030213 <--
 EP 1487801 A1 20041222 EP 2003-704631 20030213 <--
 EP 1487801 B1 20060419
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 JP 2005522452 T 20050728 JP 2003-567882 20030213 <--
 AT 323680 T 20060515 AT 2003-704631 20030213 <--
 ES 2260607 T3 20061101 ES 2003-704631 20030213 <--
 US 20050090485 A1 20050428 US 2004-503678 20040804 <--
 PRAI GB 2002-3437 A 20020213 <--
 GB 2002-4758 A 20020228 <--
 GB 2002-12548 A 20020530 <--
 GB 2002-19711 A 20020823 <--
 WO 2003-EP1543 W 20030213
 OS MARPAT 139:197390
 RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of 3-arylsulfonyl-7-piperazinyl- indoles, -benzofurans and
 -benzothiophenes with 5-HT6 receptor affinity for treating CNS disorders
 GI

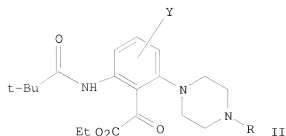
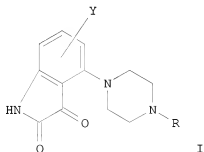


AB The title compds. I [R1, R2 = H, alkyl; or R1 is linked to R2 to form
 (CH2)2-4; R3 = H, halo, CN, etc.; R4 = H, alkyl; m = 1-4; n = 1-3; X = NH,
 N(alkyl), O, S; A = Ar1, Ar2Ar3; Ar1-Ar3 = (un)substituted (hetero)aryl],
 useful in the treatment of various disorders, including CNS disorders,
 were prepared. Thus, reacting 3-(1H-indole-1-sulfonyl)-1H-indol-7-ylamine
 (preparation given) with methlorethamine.HCl in the presence of Na2CO3 in BuOH
 afforded 40% I [R1 = Me; R2-R4 = H; X = NH; A = 1H-indol-1-yl]. The
 exemplified compds. I were tested and all (26) showed good affinity for
 the 5-HT6 receptor, having pKi values > 8.0 at human cloned 5-HT6
 receptors.
 AN 2003:133027 HCAPLUS <<LOGINID::20080822>>
 DN 138:187788
 TI Preparation of 3-arylsulfonyl-7-piperazinyl- indoles, -benzofurans and
 -benzothiophenes with 5-HT6 receptor affinity for treating CNS disorders
 IN Bromidge, Steven Mark; Johnson, Christopher Norbert; MacDonald, Gregor

James; Thompson, Mervyn; Witty, David R.
 PA Smithkline Beecham PLC, UK
 SO PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------|---|------|----------|-----------------|--------------|
| PI | WO 2003013510 | A1 | 20030220 | WO 2002-EP8719 | 20020805 <-- |
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| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2002331394 | A1 | 20030224 | AU 2002-331394 | 20020805 <-- |
| | EP 1414442 | A1 | 20040506 | EP 2002-767322 | 20020805 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | JP 2005527463 | T | 20050915 | JP 2003-518519 | 20020805 <-- |
| | US 20040242589 | A1 | 20041202 | US 2004-486068 | 20040206 <-- |
| PRAI | GB 2001-19242 | A | 20010807 | <-- | |
| | GB 2002-3300 | A | 20020212 | <-- | |
| | WO 2002-EP8719 | W | 20020805 | <-- | |
| OS | MARPAT 138:187788 | | | | |
| RE.CNT 3 | THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD | | | | |
| | ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | | |

L12 ANSWER 5 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of piperazinyI-isatins useful as selective dopamine
 autoreceptor agonists
 GI



AB Piperazinyl-isatins [I; wherein Y = H, Me, OMe, SMe, CF₃; R = H, (C1-C3)alkyl, (CH₂)_nAr (n = 0, 1 or 2) (Ar = Ph, methoxyphenyl)] were prepared by acid catalyzed cyclization of (II). For example, 4-(4-benzylpiperazin-1-yl)-1H-indole-2,3-dione [i.e., I, wherein Y = H; R = CH₂Ph] was prepared by acid catalyzed cyclization of corresponding (II) (synthetic preparation given). These compds. are selective dopamine autoreceptor agonists useful in treating disease states involving hyperactivity of dopamine systems. For example, affinity for the dopamine autoreceptor of 4-(4-benzylpiperazin-1-yl)-1H-indole-2,3-dione exhibited IC₅₀ = 0.57 nM wherein homogenized rat striatal brain tissue is incubated with [3H]-quinpirole at various concns. of test compound

AN 2002:868907 HCAPLUS <<LOGINID:20080822>>

DN 137:370107

TI Preparation of piperazinyl-isatins useful as selective dopamine autoreceptor agonists

IN Greenblatt, Lynne Padilla; Jirkovsky, Ivo; Newshaw, Richard Eric

PA Wyeth, John and Brother Ltd., USA

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 2002090327 | A1 | 20021114 | WO 2002-US14452 | 20020507 <-- |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW | | | | |
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| | US 20030013722 | A1 | 20030116 | US 2002-139695 | 20020503 <-- |
| | US 6743796 | B2 | 20040601 | | |
| | AU 2002305440 | A1 | 20021118 | AU 2002-305440 | 20020507 <-- |
| PRAI | US 2001-289171P | P | 20010507 | <-- | |
| | WO 2002-US14452 | W | 20020507 | <-- | |

OS MARPAT 137:370107

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Antipsychotic, antidepressant, anxiolytic, and anticonvulsant drugs induce type II nitric oxide synthase mRNA in rat brain

AB Nitric oxide synthase inhibitors have been regarded as potentially beneficial for psychiatric disorders such as depression and schizophrenia, though little is known about how nitric oxide synthases are affected by psychotropic drugs in the brain. Using reverse transcription-polymerase chain reaction anal., we investigated the effects of short- and long-term oral treatments with several psychotropics on type II nitric oxide synthase gene expression in the rat brain. With maprotiline and fluvoxamine, enzyme mRNA levels were higher after a 28 day treatment than after 1 and 4 day treatments. Zonisamide, carbamazepine and diazepam also increased mRNA, though differences in levels between 1, 4 and 28 day treatments were not significant. These results suggest that psychotropics modulate the gene expression of type-II nitric oxide

synthase in the brain.
 AN 2002:854661 HCAPLUS <<LOGINID:20080822>>
 DN 138:379060
 TI Antipsychotic, antidepressant, anxiolytic, and
 anticonvulsant drugs induce type II nitric oxide synthase mRNA in rat
 brain
 AU Suzuki, Eiji; Nakaki, Toshio; Shintani, Futoshi; Kanba, Shigenobu;
 Miyaoka, Hitoshi
 CS Department of Psychiatry, Kitasato University School of Medicine, 2-1-1
 Asamizodai, Sagami-hara, Kanagawa, 228-8520, Japan
 SO Neuroscience Letters (2002), 333(3), 217-219
 CODEN: NELED5; ISSN: 0304-3940
 PB Elsevier Science Ireland Ltd.
 DT Journal
 LA English
 RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Transgenic or recombinant nonhuman mammals and their applications in
 screening medicaments used in psychoactive disorders
 AB Transgenic or recombinant nonhuman mammals are made to express a gene
 coding for a microtubule-associated protein (MAP) which expression is
 modified by a STOP gene (inactivation or overexpression) so they can be
 used in screening drugs used to treat anxiety, schizophrenia,
 schizoaffective disorders, paranoia, and depression.
 AN 2002:725761 HCAPLUS <<LOGINID:20080822>>
 DN 137:210898
 TI Transgenic or recombinant nonhuman mammals and their applications in
 screening medicaments used in psychoactive disorders
 IN Andrieux, Annie; Job, Didier; Denarier, Eric; Bosc, Christophe; Vernet,
 Muriel
 PA Commissariat a l'Energie Atomique, Fr.; Institut National de la Sante et
 de la Recherche Medicale INSERM
 SO Fr. Demande, 38 pp.
 CODEN: FRXXBL
 DT Patent
 LA French
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--|------|----------|-----------------|--------------|
| PI | FR 2817117 | A1 | 20020531 | FR 2000-15240 | 20001124 <-- |
| | FR 2817117 | B1 | 20051104 | | |
| | WO 2002041691 | A2 | 20020530 | WO 2001-FR3701 | 20011123 <-- |
| | WO 2002041691 | A3 | 20030213 | | |
| | W: CA, IL, JP, US | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| | EP 1335646 | A2 | 20030820 | EP 2001-997219 | 20011123 <-- |
| | EP 1335646 | B1 | 20070117 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | ES 2280432 | T3 | 20070916 | ES 2001-997219 | 20011123 <-- |
| | US 20040093625 | A1 | 20040513 | US 2003-432241 | 20031117 <-- |
| PRAI | FR 2000-15240 | A | 20001124 | <-- | |
| | WO 2001-FR3701 | W | 20011123 | <-- | |

L12 ANSWER 8 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Management of symptoms associated with advanced cancer: olanzapine and
 mirtazapine
 AB A review. Advanced cancer patients are polysymptomatic and often receive

multiple medications for symptom relief. Common symptoms include anorexia, weight loss, delirium and depression. Olanzapine and mirtazapine may have several advantages over older agents despite increased acquisition costs. Both medications can treat several symptoms with a low risk for drug-drug interactions and with only once- or twice-daily dosing. Drug side effects are low, compared with more conventionally used agents. The pharmacokinetics and pharmacodynamics of both agents are unique and explain many of the benefits. More research and clin. experience will be necessary to define their role in the palliation of advanced cancer.

AN 2002:720957 HCAPLUS <<LOGINID:20080822>>

DN 137:272678

TI Management of symptoms associated with advanced cancer: olanzapine and mirtazapine

AU Davis, Mellar P.; Khawam, Elias; Pozuelo, Leo; Lagman, Ruth

CS Harry R. Horvitz Cent. for Palliative Med., Cleveland Clin. Found., Cleveland, OH, 44195, USA

SO Expert Review of Anticancer Therapy (2002), 2(4), 365-376

CODEN: ERATBJ; ISSN: 1473-7140

PB Future Drugs Ltd.

DT Journal; General Review

LA English

RE.CNT 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI An open pilot study combining risperidone and a selective serotonin reuptake inhibitor as initial antidepressant therapy

AB Background: Atypical antipsychotics such as risperidone or olanzapine have been reported to be effective when added to a selective serotonin reuptake inhibitor (SSRI) in cases of depression in which treatment with an SSRI alone is not effective. It is possible that the combination of an SSRI and an atypical antipsychotic may be efficacious as an initial treatment for major depression. Method: Thirty-six subjects who fulfilled DSM-IV diagnostic criteria for major depressive disorder were given fluvoxamine, 50 or 75 mg/day, with risperidone, 0.5 or 1 mg/day, at the start of treatment. The dose of fluvoxamine was increased to 100 or 150 mg/day on the fourth day of the treatment and maintained thereafter. Hamilton Rating Scale for Depression (HAM-D) scores were obtained at baseline and every week for 6 wk. Remission and response were defined, resp., as $\geq 75\%$ and 50% -74% reduction from baseline in HAM-D score. Results: Of 30 subjects who completed the 6-wk study, 23 (76%) achieved remission, 5 (17%) achieved response, and 2 (7%) were nonresponsive. Of the 6 patients who did not complete the study, 3 showed remission, 1 showed response, and 2 showed minimal or no response by the time of dropout. The reported adverse effects were mild, and none of the 36 subjects enrolled in the study manifested or reported extrapyramidal symptoms, nausea, or vomiting. Conclusion: The results suggest that the combination of risperidone and fluvoxamine from the beginning of antidepressant therapy enhances the therapeutic response rate in depression.

AN 2002:708135 HCAPLUS <<LOGINID:20080822>>

DN 137:242083

TI An open pilot study combining risperidone and a selective serotonin reuptake inhibitor as initial antidepressant therapy

AU Hirose, Shigehiro; Ashby, Charles R., Jr.

CS Center of Psychiatry and Neurology, Fukui Prefectural Hospital, Fukui, 910-0846, Japan

SO Journal of Clinical Psychiatry (2002), 63(8), 733-736

CODEN: JCLPDE; ISSN: 0160-6689

PB Physicians Postgraduate Press, Inc.

DT Journal
LA English

RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Focus on amisulpride

AB A review. Amisulpride is a second-generation antipsychotic, a substituted benzamide. It appears to be an effective agent in treating schizophrenia for what are characterized as pos. and neg. symptoms. The recommended doses are between 400 mg/day and 800 mg/day. Amisulpride demonstrates a good global safety profile, particularly when compared with first-generation antipsychotics, such as haloperidol. There are interesting studies that point towards amisulpride's antidepressant effect in dysthymia speculative on possible roles in affective psychoses and chronic fatigue syndrome.

AN 2002:690705 HCAPLUS <<LOGINID:20080822>>

DN 137:226106

TI Focus on amisulpride

AU Green, Ben

CS University of Liverpool, UK

SO Current Medical Research and Opinion (2002), 18(3), 113-117

CODEN: CMROCX; ISSN: 0300-7995

PB LibraPharm Ltd.

DT Journal; General Review

LA English

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI The gerbil elevated plus-maze. I. Behavioral characterization and pharmacological validation

AB Several neurokinin NK1 receptor antagonists currently being developed for anxiety and depression have reduced affinity for the rat and mouse NK1 receptor compared with human. Consequently, it has proven difficult to test these agents in traditional rat and mouse models of anxiety and depression. This issue has been overcome, in part, by using non-traditional laboratory species such as the guinea pig and gerbil, which have NK1 receptors closer in homol. to human NK1 receptors. However, there are very few reports describing the behavior of gerbils in traditional models of anxiety. The aim of the present study was to determine if the elevated plus-maze, a commonly used anxiety model, could be adapted for the gerbil. Using a specially-designed elevated plus-maze, gerbils exhibited an 'anxious' behavioral profile similar to that observed in rats and mice, i.e., reduced entries into, and time spent exploring, an open, aversive arm. The anxiolytic drugs diazepam (0.03-3 mg/kg i.p.), chlordiazepoxide (0.3-10 mg/kg i.p.), and buspirone (0.3-30 mg/kg s.c.) increased open arm exploration and produced anxiolytic-like effects on risk-assessment behaviors (reduced stretch-attend postures and increased head dips). Of particular interest, the antidepressant drugs imipramine (1-30 mg/kg p.o.), fluoxetine (1-30 mg/kg, p.o.) and paroxetine (0.3-10 mg/kg p.o.) each produced some acute anxiolytic-like activity, without affecting locomotor activity. The antipsychotic, haloperidol, and the psychostimulant, amphetamine, did not produce any anxiolytic-like effects (1-10 mg/kg s.c.). The anxiogenic β -carboline, FG-7142, reduced time spent in the open arm and head dips, and increased stretch-attend postures (1-30 mg/kg, i.p.). These studies have demonstrated that gerbils exhibit an anxiety-like profile on an elevated plus-maze, and that the gerbil elevated plus-maze may have predictive validity for anxiolytics, and antidepressants with potential anxiolytic-like effects.

AN 2002:681899 HCAPLUS <<LOGINID::20080822>>
DN 138:296994
TI The gerbil elevated plus-maze. I. Behavioral characterization and pharmacological validation
AU Varty, Geoffrey B.; Morgan, Cynthia A.; Cohen-Williams, Mary E.; Coffin, Vicki L.; Carey, Galen J.
CS CNS Biological Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SO Neuropsychopharmacology (2002), 27(3), 357-370
CODEN: NEROEW; ISSN: 0893-133X
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Pharmacology of flibanserin
AB A review. Flibanserin has preferential affinity for serotonin 5-HT1A, dopamine D4, and serotonin 5-HT2A receptors. In vitro and in microiontophoresis, flibanserin behaves as a 5-HT1A agonist, a very weak partial agonist on dopamine D4 receptors, and a 5-HT2A antagonist. In vivo flibanserin binds equally to 5-HT1A and 5-HT2A receptors. However, under higher levels of brain 5-HT (i.e., under stress), flibanserin may occupy 5-HT2A receptors in higher proportion than 5-HT1A receptors. The effects of flibanserin on adenylyl cyclase are different from those of buspirone and 8-OH-DPAT, two other purported 5-HT1A receptor agonists. Flibanserin reduces neuronal firing rate in cells of the dorsal raphe, hippocampus, and cortex with the CA1 region being the most sensitive in the brain. Flibanserin-induced reduction in firing rate in the cortex seems to be mediated through stimulation of postsynaptic 5-HT1A receptors, whereas the reduction of the number of active cells seems to be mediated through dopamine D4 receptor stimulation. Flibanserin quickly desensitizes somatic 5-HT autoreceptors in the dorsal raphe and enhances tonic activation of postsynaptic 5-HT1A receptors in the CA3 region. Flibanserin preferentially reduces synthesis and extracellular levels of 5-HT in the cortex, where it enhances extracellular levels of NE and DA. Flibanserin displays antidepressant-like activity in most animal models sensitive to antidepressants. Such activity, however, seems qualitatively different from that exerted by other antidepressants. Flibanserin seems to act via direct or indirect stimulation of 5-HT1A, DA, and opioid receptors in those animal models. Flibanserin does not display consistent effects in animal models of anxiety and seems to exert potential antipsychotic effects. Flibanserin may induce some sedation but does not induce observable toxic effects at pharmacologically relevant doses.

AN 2002:679189 HCAPLUS <<LOGINID::20080822>>
DN 138:231158
TI Pharmacology of flibanserin
AU Borsini, Franco; Evans, Kenneth; Jason, Kathryn; Rohde, Frank; Alexander, Barbara; Pollentier, Stephan
CS Boehringer Ingelheim Pharma KG, Biberach an der Riss, 88397, Germany
SO CNS Drug Reviews (2002), 8(2), 117-142
CODEN: CDREFB; ISSN: 1080-563X
PB Neva Press
DT Journal; General Review
LA English
RE.CNT 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Inhibition of risperidone metabolism by fluoxetine in patients with
 AB schizophrenia: A clinically relevant pharmacokinetic drug interaction
 The effect of fluoxetine on the steady-state plasma concns. of risperidone
 and its active metabolite 9-hydroxyrisperidone (9-OH-risperidone) was
 evaluated in 10 patients with schizophrenia or schizo affective disorder.
 Patients stabilized on risperidone (4-6 mg/day) received addnl. fluoxetine
 (20 mg/day) to treat concomitant depression. One patient
 dropped out after 1 wk due to the occurrence of akathisia associated with
 markedly increased plasma risperidone concns. In the other subjects, mean
 plasma concns. of risperidone increased during fluoxetine administration
 from 12 ± 9 ng/mL at baseline to 56 ± 31 at week 4 ($p < 0.001$),
 while the levels of 9-OH-risperidone were not significantly affected.
 After 4 wk of combined treatment, the levels of the active moiety (sum of
 the concns. of risperidone and 9-OH-risperidone) increased by 75% (range,
 9-204%, $p < 0.01$) compared with baseline. The mean plasma
 risperidone/9-OH-risperidone ratio also increased significantly. During
 the second week of adjunctive therapy, two patients developed Parkinsonian
 symptoms, which were controlled with anticholinergic medication. These
 findings indicate that fluoxetine, a potent inhibitor of the cytochrome P
 450 enzyme CYP2D6 and a less potent inhibitor of CYP3A4, reduces the
 clearance of risperidone by inhibiting its 9-hydroxylation or alternative
 metabolic pathways. This interaction may lead to toxic plasma risperidone
 concns. In addition to careful clin. observation, monitoring plasma
 risperidone levels may be of value in patients given adjunctive therapy
 with fluoxetine.

AN 2002:652311 HCAPLUS <<LOGINID:20080822>>

DN 137:195009

TI Inhibition of risperidone metabolism by fluoxetine in patients with
 schizophrenia: A clinically relevant pharmacokinetic drug interaction
 AU Spina, Edoardo; Avenoso, Angela; Scordo, Maria Gabriella; Ancione, Maria;
 Madaia, Aldo; Gatti, Giuliana; Perucca, Emilio
 CS Department of Clinical and Experimental Medicine and Pharmacology, Section
 of Pharmacology, University of Messina, Messina, 98125, Italy
 SO Journal of Clinical Psychopharmacology (2002), 22(4), 419-423
 CODEN: JCPYDR; ISSN: 0271-0749

PB Lippincott Williams & Wilkins

DT Journal

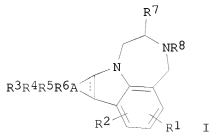
LA English

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Preparation of diazepinocarbazoles and related compounds as serotonin
 5-HT2C agonists.

GI



AB A method of treatment of obsessive-compulsive disorder, obesity, eating

disorders, sleeping disorders, migraine, depression, generalized anxiety disorder, schizophrenia, panic disorder, migraine, epilepsy or anxiety in a mammal, the method comprises administration of title compds. (I; A = 6-8 membered cycloalkyl ring; R1, R2 = H, alkyl, cycloalkyl, cycloalkylmethyl, alkoxy, halo, fluoroalkyl, cyano, alkylaminosulfonyl, amino, fluoroalkoxy, aroyl, heteroaroyl etc.; R3-R6 = H, alkyl, cycloalkyl, cycloalkylmethyl, alkoxy, cycloalkoxy; R7, R8 = H, alkyl; dashed line = optional double bond). Thus, 4-acetyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine (preparation given) in aqueous HCl was treated with NaNO2

under ice cooling to give an oil which in HOAc was treated with Zn. The resulting mixture was filtered into a flask containing cyclohexanone followed by

heating for 1.5 h to give 3-acetyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,7,1-jk]carbazole. The latter was refluxed 4 h with concentrate HCl to give 1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,7,1-jk]carbazole hydrochloride. This reduced food intake in rats with ED50 = 20.86 mg/kg i.p.

AN 2002:353459 HCAPLUS <<LOGINID:20080822>>

DN 136:355252

TI Preparation of diazepinocarbazoles and related compounds as serotonin 5-HT2C agonists.

IN Sabb, Annmarie Louise; Vogel, Robert Lewis; Welmaker, Gregory Scott; Sabalski, Joan Eileen

PA John Wyeth and Brother Ltd., USA

SO PCT Int. Appl., 47 pp.

CODEN: PIXXD2

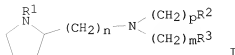
DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 2002036596 | A2 | 20020510 | WO 2001-US46084 | 20011101 <-- |
| | WO 2002036596 | A3 | 20021024 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 2002027170 | A | 20020515 | AU 2002-27170 | 20011101 <-- |
| | US 20020086860 | A1 | 20020704 | US 2001-17738 | 20011102 <-- |
| | US 6503900 | B2 | 20030107 | | |
| | US 20020119966 | A1 | 20020829 | US 2001-16228 | 20011102 <-- |
| | US 6759405 | B2 | 20040706 | | |
| | US 20020128261 | A1 | 20020912 | US 2001-16743 | 20011102 <-- |
| | US 6858604 | B2 | 20050222 | | |
| | US 20040229865 | A1 | 20041118 | US 2004-872090 | 20040618 <-- |
| | US 7271162 | B2 | 20070918 | | |
| | US 20050054635 | A1 | 20050310 | US 2004-966227 | 20041015 <-- |
| | US 7271164 | B2 | 20070918 | | |
| PRAI | US 2000-245598P | P | 20000103 | <-- | |
| | US 2000-245599P | P | 20000103 | <-- | |
| | US 2000-245602P | P | 20000103 | <-- | |
| | WO 2001-US46084 | W | 20011101 | <-- | |
| | US 2001-16228 | A1 | 20011102 | <-- | |
| | US 2001-16743 | A1 | 20011102 | <-- | |
| OS | MARPAT 136:355252 | | | | |

L12 ANSWER 15 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of aminoalkylpyrrolidines as serotonin 5-HT₇ receptor ligands.
 GI



AB Title compds. [I; m, n, p = 1, 2; R1 = alkyl; R2, R3 = (substituted) aryl, heteroaryl, aralkyl, heteroarylalkyl, cycloalkenyl; when R1 = Et and m, n, p = 1, R2, R3 ≠ Ph], were prepared I are useful for treating sleep disorders, pain, depression, and schizophrenia. Thus, NaBH₃CN in CF₃CO₂H was added to a mixture of (S)-2-(2-aminoethyl)-1-methylpyrrolidine (preparation given) and 3-hydroxybenzaldehyde in MeOH followed by stirring for 48 h to give (S)-2-[2-[bis-(3-hydroxybenzyl)amino]ethyl]-N-methylpyrrolidine. The latter bound to 5-HT₇ receptors with K_i = 9.7 nM.

AN 2002:353424 HCAPLUS <<LOGINID:20080822>>

DN 136:369601

TI Preparation of aminoalkylpyrrolidines as serotonin 5-HT₇ receptor ligands.

IN Rui, Yuanjin; Kuki, Atsuo; Hong, Yufeng; Peng, Zhengwei; Luthin, David Robert

PA Warner-Lambert Company, USA

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 2002036560 | A1 | 20020510 | WO 2001-IB2023 | 20011026 <-- |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2425286 | A1 | 20020510 | CA 2001-2425286 | 20011026 <-- |
| | AU 2001095837 | A | 20020515 | AU 2001-95837 | 20011026 <-- |
| | EP 1339677 | A1 | 20030903 | EP 2001-976572 | 20011026 <-- |
| | EP 1339677 | B1 | 20060104 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | BR 2001015042 | A | 20040203 | BR 2001-15042 | 20011026 <-- |
| | JP 2004517058 | T | 20040610 | JP 2002-539320 | 20011026 <-- |
| | AT 315023 | T | 20060215 | AT 2001-976572 | 20011026 <-- |
| | ES 2251514 | T3 | 20060501 | ES 2001-976572 | 20011026 <-- |
| | MX 2003PA02595 | A | 20030630 | MX 2003-PA2595 | 20030325 <-- |
| | US 20040039044 | A1 | 20040226 | US 2003-415546 | 20030429 <-- |
| | US 20060063932 | A1 | 20060323 | US 2005-229816 | 20050919 <-- |
| PRAI | US 2000-243710P | P | 20001030 | <-- | |
| | WO 2001-IB2023 | W | 20011026 | <-- | |

US 2003-415546 A1 20030429
 OS MARPAT 136:369601
 RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Use of cortisol-sequestering agents for the treatment of hypercortisolemia-related disorders
 AB The invention relates to the use of sequestering agents for the preparation of a medicament for the treatment of hypercortisolemia-related disorders, especially for the treatment of major depression; to pharmaceutical compns. comprising a cortisol-sequestering agent, and to the cortisol-sequestering agent 6-per-deoxy-6-per-(2,3-dihydroxypropylthio)- γ -cyclodextrin.
 AN 2002:353267 HCAPLUS <<LOGINID:20080822>>
 DN 136:363859
 TI Use of cortisol-sequestering agents for the treatment of hypercortisolemia-related disorders
 IN Zhang, Mingquiang; Hill, David Robert; Rees, David
 PA Akzo Nobel N.V., USA
 SO PCT Int. Appl., 14 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|--------------|
| PI | WO 2002036105 | A2 | 20020510 | WO 2001-EP12267 | 20011030 <-- |
| | WO 2002036105 | A3 | 20021031 | | |
| | W: | AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GE, GR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | AU 2002020654 | A | 20020515 | AU 2002-20654 | 20011030 <-- |
| | EP 1333842 | A2 | 20030813 | EP 2001-992568 | 20011030 <-- |
| | EP 1333842 | B1 | 20060830 | | |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| | JP 2004512358 | T | 20040422 | JP 2002-538917 | 20011030 <-- |
| | EP 1629845 | A2 | 20060301 | EP 2005-111297 | 20011030 <-- |
| | EP 1629845 | A3 | 20060322 | | |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR | | | |
| | AT 337790 | T | 20060915 | AT 2001-992568 | 20011030 <-- |
| | ES 2269504 | T3 | 20070401 | ES 2001-992568 | 20011030 <-- |
| | US 20040048830 | A1 | 20040311 | US 2003-415867 | 20030902 <-- |
| PRAI | EP 2000-309725 | A | 20001102 | <-- | |
| | EP 2001-992568 | A3 | 20011030 | <-- | |
| | WO 2001-EP12267 | W | 20011030 | <-- | |

L12 ANSWER 17 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Serotonin reuptake inhibition: An update on current research strategies
 AB A review. Selective Serotonin reuptake inhibitors (SSRIs) have contributed to the major advances in the treatment of depression and other psychiatric diseases. This review is on the current knowledge concerning the SSRI class of drugs and discusses the importance of secondary pharmacol. in the mechanism of action and effectiveness of these

drugs. Particular attention is given to the emerging importance of the SSRI "plus" approach: where the serotonin reuptake receptor inhibition of a drug is supplemented by one or more other receptor interactions either by the same drug or by a combination therapy. This area of research has shed light on the pharmacol. mechanisms of SSRI therapy and has the therapeutic usefulness of serotonin reuptake inhibition, especially in the area of depression. There are many new emerging SSRI "plus" drugs, which address the pharmacol. and pharmacokinetic issues of current therapies and these, are discussed in detail.

AN 2002:335884 HCAPLUS <<LOGINID:20080822>>
DN 137:288312

TI Serotonin reuptake inhibition: An update on current research strategies
AU Spinks, D.; Spinks, G.
CS Department of Medicinal Chemistry, Organon Laboratories Ltd., Lanarkshire, ML1 5SH, UK
SO Current Medicinal Chemistry (2002), 9(8), 799-810
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers
DT Journal; General Review
LA English

RE.CNT 120 THERE ARE 120 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Method for the treatment of neurological and neuropsychological disorders
AB The present invention discloses a method for therapeutically treating an animal, including a human, for psychosomatic, depressive and neuropsychiatric diseases, such as anxiety, depression, insomnia, schizophrenia, epilepsy, spasm and chronic pain. Administration of a suitable attractin inhibitor causes the reduction of activity in the enzyme attraction or in isoforms thereof in the brain of mammals and leads as a causal consequence to a reduced degradation of the neuropeptide Y (NPY) and similar substrates. Such treatment will result in a reduction or delay in the decrease of the concentration of functionally active neuronal NPY(1-36).

As a consequence of the resulting enhanced stability of the endogenous NPY(1-36), NPY activity is prolonged thereby resulting among other things in functionally active NPY Y1 receptor activity thereby facilitating antidepressive, anxiolytic, analgesic, antihypertension and other neurol. effects.

AN 2002:332016 HCAPLUS <<LOGINID:20080822>>
DN 136:345801

TI Method for the treatment of neurological and neuropsychological disorders
IN Von Hoersten, Stephan; Hoffmann, Torsten; Demuth, Hans-Ulrich;
Kuehn-Wache, Kerstin; Friedrich, Daniel
PA Probiobdrug Ag, Germany
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|--------------|
| PI | WO 2002034242 | A2 | 20020502 | WO 2001-EP12478 | 20011029 <-- |
| | WO 2002034242 | A3 | 20030130 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | |

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| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG | |
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| CA | 2424475 | A1 | 20020502 CA 2001-2424475 20011029 <-- |
| AU | 2002027898 | A | 20020506 AU 2002-27898 20011029 <-- |
| EP | 1328270 | A2 | 20030723 EP 2001-988582 20011029 <-- |
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| ZA | 2003002590 | A | 20040402 ZA 2003-2590 20011029 <-- |
| JP | 2004512299 | T | 20040422 JP 2002-537296 20011029 <-- |
| EP | 1891948 | A1 | 20080227 EP 2007-122835 20011029 <-- |
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| CN | 101143217 | A | 20080319 CN 2006-10121911 20011029 <-- |
| AT | 399008 | T | 20080715 AT 2001-988583 20011029 <-- |
| IN | 2003MN00357 | A | 20070608 IN 2003-MN357 20030331 <-- |
| NO | 2003001849 | A | 20030623 NO 2003-1849 20030424 <-- |
| US | 20040043919 | A1 | 20040304 US 2003-415263 20030826 <-- |
| AU | 2006201186 | A1 | 20060413 AU 2006-201186 20060322 <-- |
| AU | 2006201186 | B2 | 20070405 |
| US | 20060252701 | A1 | 20061109 US 2006-397281 20060404 <-- |
| PRAI | US 2000-244036P | P | 20001027 <-- |
| US | 2001-14291 | A1 | 20011026 <-- |
| AU | 2002-221773 | A3 | 20011029 <-- |
| CN | 2001-818067 | A3 | 20011029 <-- |
| EP | 2001-988583 | A3 | 20011029 <-- |
| WO | 2001-EP12478 | W | 20011029 <-- |

L12 ANSWER 19 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Modulation of neuronal activities in the central nervous system via sigma receptors

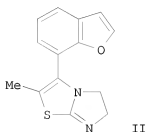
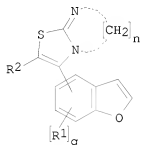
AB A review. Sigma receptors have recently been the target of drug development related to psychiatric disorders, including schizophrenia and depression, as well as cognitive enhancers. This paper focused on the sigma-receptor-mediated modulation of neuronal activity, especially the effects on aminergic neuron and hippocampal neuron activity. Dopaminergic neuron activities in the substantia nigra and ventral tegmental area (VTA) are variously modified by the systemic administration of sigma ligands. When applied with microiontophoresis, they are reported to increase dopaminergic neuron activity in the VTA. This activity may be involved in the psychotropic or antipsychotic effects of these ligands. Moreover, serotonergic neurons in the raphe nucleus and noradrenergic neurons in the locus coeruleus were activated by sigma ligands. These effects are probably related to the antidepressant activity of sigma receptor ligands. In the hippocampus, sigma ligands suppressed CA1 neuronal activity in vitro. The effects were suggested to be due to an increase in the threshold of action potential and decreased synaptic transmission efficacy. NMDA receptor function was modified in biphasic fashion related to doses of sigma ligands, i.e., a lower dose facilitated the NMDA receptor functions, and a higher dose inhibited them. These effects on the hippocampal neurons may contribute to their neuroprotective and anti-amnesic actions. Further studies are needed to elucidate the relation between the physiological function of sigma receptor and psychiatric diseases by the use of sigma receptor ligands and molecular techniques.

AN 2002:317619 HCAPLUS <<LOGINID:20080822>>

DN 137:57627

TI Modulation of neuronal activities in the central nervous system via sigma

receptors
 AU Ishihara, Kumatoshi; Sasa, Masashi
 CS Department of Pharmacotherapy, Graduate School of Medical Sciences,
 Hiroshima University, Hiroshima, 734-8551, Japan
 SO Nippon Shinkei, Seishin Yakurigaku Zasshi (2002), 22(1), 23-30
 CODEN: NSSZEW; ISSN: 1340-2544
 PB Nippon Shinkei Seishin Yakuri Gakkai
 DT Journal; General Review
 LA Japanese
 L12 ANSWER 20 OF 72 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI Preparation of dihydroimidazo[2,1-b]thiazoles and dihydro-5H-thiazolo[3,2-
 a]pyrimidines with 5-HT receptor affinity
 GI



AB The title compds. [I; g = 0-5; n = 2-3; R₁ = halo, alkyl, alkoxy, etc.; R₂ = H, alkyl, hydroxyalkyl, etc.; the condensed thiazole ring is attached at the 4,5,6 or 7-position of the benzofuran ring] which have affinity for 5-HT_{1A} receptors and which inhibit neuronal re-uptake of 5-hydroxytryptamine and/or noradrenaline, to processes for their preparation, to pharmaceutical compns. containing them and to their use in the treatment of depression, anxiety, psychoses (for example schizophrenia), tardive dyskinesia, obesity, drug addiction, drug abuse, cognitive disorders, Alzheimer's disease, obsessive-compulsive behavior, panic attacks, social phobias, eating disorders such as bulimia, anorexia, snacking and binge eating, non-insulin dependent diabetes mellitus, hyperglycemia, hyperlipidemia, stress, as an aid to smoking cessation and in the treatment and/or prophylaxis of seizures, neurol. disorders such as epilepsy and/or conditions in which there is neurol. damage such as stroke, brain trauma, cerebral ischemia, head injuries and hemorrhage, were prepared and formulated. Thus, treating 1-(benzo[b]furan-7-yl)propan-1-one (preparation given) with phenyltrimethylammonium tribromide in THF followed by reaction of the intermediate with 2-imidazolidinethione in the presence of AcOH in EtOH afforded II.HBr which showed K_i of 28 nM against 5-HT_{1A} binding.
 AN 2002:256267 HCAPLUS <<LOGINID:20080822>>
 DN 136:279473
 TI Preparation of dihydroimidazo[2,1-b]thiazoles and dihydro-5H-thiazolo[3,2-
 a]pyrimidines with 5-HT receptor affinity
 IN Brough, Paul; Watts, John Paul; Cockroft, Victor; Kerrigan, Frank; Doyle, Kevin James
 PA Knoll G.m.b.H., Germany
 SO PCT Int. Appl., 66 pp.
 CODEN: PIXXD2
 DT Patent
 LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| WO 2002026747 | A1 | 20020404 | WO 2001-GB4317 | 20010927 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2001090126 A5 20020408 AU 2001-90126 20010927 <-- PRAI GB 2000-23610 A 20000927 <-- WO 2001-GB4317 W 20010927 <-- OS MARPAT 136:279473 RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | | |

=> file hcaplus
 COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
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| ENTRY | SESSION |
| 0.21 | 0.21 |

FULL ESTIMATED COST

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FILE COVERS 1907 - 25 Aug 2008 VOL 149 ISS 9
 FILE LAST UPDATED: 24 Aug 2008 (20080824/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s antidepressant
 L1 23140 ANTIDEPRESSANT

=> s antipsychotic
 L2 11265 ANTIPSYCHOTIC

=> s suicide
 L3 7101 SUICIDE

=> s 12 and 12 and 13
L4 79 L2 AND L2 AND L3

=> s MDD or (major depressive disorder) or unipolar
857 MDD
708684 MAJOR
9838 DEPRESSIVE
276785 DISORDER
1518 MAJOR DEPRESSIVE DISORDER
(MAJOR(W)DEPRESSIVE(W)DISORDER)
4106 UNIPOLAR
L5 5875 MDD OR (MAJOR DEPRESSIVE DISORDER) OR UNIPOLAR

=> s 14 and 15
L6 9 L4 AND L5

=> d 16 1-9 ti abs bib

L6 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Hemoperfusion in the treatment of acute clozapine intoxication in China
AB Background and Aims: No systematic study has focused on the characteristics and outcome of acute clozapine intoxication, although clozapine is the most widely used antipsychotic agent in China. The study reported herein examined the features of clozapine intoxication and the therapeutic effect of hemoperfusion (HP). Methods: In a retrospective chart review, the notes of 47 patients who attempted suicide by ingesting large amts. of clozapine and were treated at the only psychiatric emergency service in Beijing were analyzed. Of the 20 unconscious patients with plasma clozapine concns. of more than 2000 ng/mL, 14 received a combination of HP and symptomatic treatment, whereas the other 6 and the remaining 27 patients received only symptomatic treatment. Patients' psychiatric conditions and both plasma clozapine and norclozapine concns. were closely monitored and registered. Results: One patient died of pulmonary edema and subsequent heart failure, but the rest of the patients recovered without any sequelae. Patients who received HP regained consciousness significantly faster than their counterparts with the same level of clozapine plasma concentration (>2000 ng/mL) who did not receive HP. Conclusions: A combination of HP and symptomatic treatment is the best therapeutic option when plasma clozapine concentration is high.

AN 2008:2164 HCAPLUS <<LOGINID::20080825>>
DN 148:253999

TI Hemoperfusion in the treatment of acute clozapine intoxication in China
AU He, Jia-Li; Xiang, Yu-Tao; Li, Wen-Biao; Cai, Zhuo-Ji; Ungvari, Gabor Sandor
CS Beijing Anding Hospital, Capital Medical University, Beijing, Peop. Rep. China

SO Journal of Clinical Psychopharmacology (2007), 27(6), 667-671
CODEN: JCPYDR; ISSN: 0271-0749

PB Lippincott Williams & Wilkins

DT Journal

LA English

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
TI Quetiapine adjunct to selective serotonin reuptake inhibitors or venlafaxine in patients with major depression, comorbid anxiety, and residual depressive symptoms: a randomized, placebo-controlled pilot study
AB This double-blind, placebo-controlled study examined the efficacy and tolerability of quetiapine in combination with selective serotonin

reuptake inhibitors (SSRIs)/venlafaxine in 58 patients with major depressive disorder, comorbid anxiety symptoms (HAM-A-14 score ≥ 14), and residual depressive symptoms (HAM-D-17 score ≥ 18 , CGI-S score ≥ 4). Patients had received an SSRI/venlafaxine (at a predefined therapeutic dose) for ≥ 6 wk. Overall, 62% (18/29) of quetiapine- and 55% (16/29) of placebo-treated patients completed the study. The mean change in HAM-D and HAM-A total scores from baseline to Week 8 (primary endpoint) was significantly greater with quetiapine (mean dose 182 mg/day) than placebo: -11.2 vs. -5.5 ($P = .008$) and -12.5 vs. -5.9 ($P = .002$), resp. The onset of quetiapine efficacy (HAM-D/HAM-A/CGI-I) was rapid (by Week 1) and continued through to Week 8. Significant differences ($P < .05$) from baseline to Week 8 were observed between groups in 7/17 HAM-D (including feelings of guilt, suicide) and 6/14 HAM-A items (including tension, cardiovascular symptoms). Response ($\geq 50\%$ decrease in total score) was higher for quetiapine than placebo: HAM-D, 48% vs. 28% (not significant, NS); HAM-A, 62% vs. 28% ($P = .02$). Remission (total score ≤ 7) was higher for quetiapine than placebo: HAM-D, 31% vs. 17% (NS); HAM-A, 41% vs. 17% (NS). CGI-S, CGI-I, and the Global Assessment Scale showed that quetiapine was significantly more effective than placebo. For quetiapine, adverse events (AEs) were similar to those previously observed; sedation/somnolence/lethargy was the most commonly reported. Here quetiapine was shown to be effective as augmentation of SSRI/venlafaxine therapy in patients with major depression, comorbid anxiety, and residual depressive symptoms, with no unexpected tolerability issues. Further studies are warranted.

AN 2007:1464191 HCAPLUS <<LOGINID:20080825>>

DN 148:253966

TI Quetiapine adjunct to selective serotonin reuptake inhibitors or venlafaxine in patients with major depression, comorbid anxiety, and residual depressive symptoms: a randomized, placebo-controlled pilot study
 AU McIntyre, Alexander; Gendron, Alain; McIntyre, Amanda
 CS Department of Psychiatry, Penticton Regional Hospital, Penticton, BC, Can.
 SO Depression and Anxiety (2007), 24(7), 487-494
 CODEN: DEANF5; ISSN: 1091-4269

PB Wiley-Liss, Inc.

DT Journal

LA English

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2008 ACS ON STN

T1 Escitalopram therapy for major depression and anxiety disorders

AB BACKGROUND: Randomized controlled clin. trials have demonstrated that escitalopram is efficacious in a range of mood and anxiety disorders, but the individual trials are insufficiently large to allow a full exploration of its tolerability. OBJECTIVE: To assess the tolerability and safety of escitalopram through anal. of all randomized controlled clin. trials in major depressive disorder and anxiety disorders. METHODS: Analyses of tolerability were based on data from all available randomized, double-blind, controlled studies completed by Dec. 2006 in which escitalopram was compared with placebo or active compds. (citalopram, fluoxetine, paroxetine, sertraline, venlafaxine). Adverse events (AEs) that occurred more frequently with escitalopram than with placebo were listed, and tolerability and safety were evaluated. RESULTS: Nausea was the only AE with an incidence greater than or equal to 10% and 5 percentage points greater than with placebo during short-term treatment. In general, AEs were mild to moderate in severity. AEs related to sexual dysfunction were similarly frequent with escitalopram and citalopram, but were higher with paroxetine. No suicide occurred among escitalopram-treated patients, and there were no significant differences

between escitalopram and placebo in incidence of suicidal behavior, measured by self-harm and suicidal thoughts. The 8 wk withdrawal rate due to AEs was higher with escitalopram than with placebo (7.3% vs 2.8%; $p < 0.001$) but lower than with paroxetine (6.6% vs 9.0%; $p < 0.01$) or venlafaxine (6.1% vs 13.2%; $p < 0.01$) (Fisher's Exact test, 2 tailed). Compared with paroxetine, escitalopram resulted in significantly fewer discontinuation symptoms (average increase in Discontinuation Emergent Signs and Symptoms Scale of 1.6 vs 3.9; $p < 0.01$). There were no clin. relevant changes in clin. laboratory values in patients treated with escitalopram. Mean weight change after 6 mo of treatment with escitalopram (0.58 ± 2.63 kg) was similar to that with placebo (0.15 ± 2.33 kg). The incidence of cardiovascular events was similar to that with placebo. The risk of AEs was no higher in special patient populations, such as the elderly (≥ 65 y of age) or those with hepatic dysfunction. CONCLUSIONS: Based on data from randomized controlled trials involving more than 4000 escitalopram-treated patients, escitalopram (10-20 mg/day) is safe and well tolerated in short- and long-term treatment.

AN 2007:1199111 HCAPLUS <<LOGINID:20080825>>

DN 148:69902

TI Escitalopram therapy for major depression and anxiety disorders

AU Baldwin, David S.; Reines, Elin Heldbo; Guiton, Christina; Weiller, Emmanuelle

CS Clinical Neuroscience Division, Royal South Hants Hospital, University Department of Mental Health, Southampton, UK

SO Annals of Pharmacotherapy (2007), 41(10), 1583-1592

CODEN: APHRER; ISSN: 1060-0280

PB Harvey Whitney Books Co.

DT Journal

LA English

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2008 ACS ON STN

TI Combination therapy for depression, prevention of suicide, and various medical and psychiatric conditions

AB The present invention relates to a new method of treatment for persons meeting diagnoses for major depressive disorder, or other unipolar (non-bipolar, nonpsychotic and non-treatment resistant) depression. The method comprises administering a combination of two categories of drugs, antipsychotics or dopamine system stabilizers, in combination with a newer antidepressant such as a selective serotonin reuptake inhibitor, as initial treatment or as soon as possible. The method targets the prevention of suicide, and provides other benefits including preventing disease progression development of tolerance toward the antidepressants. Another aspect of the invention relates to using the method for alleviating cognitive distortion and related functional impairment or health risks, and/or using the method for smoking cessation or nicotine withdrawal.

AN 2004:100942 HCAPLUS <<LOGINID:20080825>>

DN 140:139528

TI Combination therapy for depression, prevention of suicide, and various medical and psychiatric conditions

IN Migaly, Peter

PA USA

SO PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|-------|-----------------|-------|
| ----- | ---- | ----- | ----- | ----- |

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|------|-----|--|----|----------|----|--------------|----------|
| PI | WO | 2004010932 | A2 | 20040205 | WO | 2003-US23326 | 20030725 |
| | WO | 2004010932 | A3 | 20040722 | | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, HU, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| | CA | 2529857 | A1 | 20040205 | CA | 2003-2529857 | 20030725 |
| | AU | 2003268026 | A1 | 20040216 | AU | 2003-268026 | 20030725 |
| | US | 20040204401 | A1 | 20041014 | US | 2003-627358 | 20030725 |
| | EP | 1551393 | A2 | 20050713 | EP | 2003-748977 | 20030725 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| | MX | 2005PA00294 | A | 20050819 | MX | 2005-PA294 | 20050104 |
| PRAI | US | 2002-319436P | P | 20020730 | | | |
| | US | 2003-627358 | A | 20030725 | | | |
| | WO | 2003-US23326 | W | 20030725 | | | |

L6 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI Atypical antipsychotics and suicide in mood and anxiety disorders

AB A review. Globally, a million people commit suicide every year, and 10-20 million attempt it. Mood disorders, especially major depressive disorder (MDD) and bipolar disorder, are the most common psychiatric conditions associated with suicide. Primary (psychiatric and phys. illness), secondary (psychosocial), and tertiary (demog.) risk factors for suicide have been identified. Comorbid psychiatric illness, particularly anxiety symptoms or disorders, significantly increase the risk of suicidal behavior. Current standard risk assessments and precautions may be of limited value, while assessing the severity of anxiety and agitation may be more effective in identifying patients at risk. Lithium is the medication that has most consistently demonstrated an antisuicidal effect. The effects of antidepressants and conventional antipsychotics on suicide risk are uncertain, but atypical antipsychotics appear promising. Atypical antipsychotics have beneficial effects on depressed mood both in patients with MDD and in patients with bipolar disorder. In addition, data in patients with schizophrenia have demonstrated a significant improvement in the incidence of suicidal behavior with clozapine compared with olanzapine. Electroconvulsive therapy appears to have an acute benefit on suicidality.

AN 2004:21462 HCAPLUS <<LOGINID::20080825>>

DN 140:86936

TI Atypical antipsychotics and suicide in mood and anxiety disorders

AU Sharma, Verinder

CS University of Western Ontario, London, ON, Can.

SO Bipolar Disorders (2003), 5(Suppl. 2), 48-52

CODEN: BDIIAU; ISSN: 1398-5647

PB Blackwell Publishing Ltd.

DT Journal; General Review

LA English

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN

TI The role of atypical antipsychotics in bipolar depression and anxiety disorders

AB A review. Bipolar disorder is a complex condition that includes symptoms of mania, depression, and often anxiety. Diagnosing and treating bipolar depression is challenging, with the disorder often being diagnosed as unipolar depression. In addition, comorbid anxiety can be a significant detractor to successful outcomes, increasing symptom severity, frequency of episodes and suicide rates, and decreasing response to antidepressant therapy. Anxiety often precedes and hastens the onset of bipolar disorder, and a shared genetic etiol. has been suggested. Studies have demonstrated the efficacy of atypical antipsychotics for the acute and maintenance treatment of mania. Evidence from studies in patients with treatment-resistant major depressive disorder and bipolar depression indicate that these agents may also have antidepressant effects. In open trials in patients with bipolar mania, risperidone therapy has led to significant redns. in depression scores compared with baseline. Redns. in depression scores in patients with bipolar mania have been significantly greater with olanzapine compared with placebo. In patients with bipolar depression, the combination of olanzapine and fluoxetine resulted in significant improvement in depression compared with olanzapine alone or placebo. Although little data are available on the effects of these agents on comorbid anxiety in patients with bipolar disorder, some atypical antipsychotics have demonstrated efficacy in patients with anxiety disorders, including obsessive-compulsive disorder, post-traumatic stress disorder, and generalized anxiety disorder. Thus, atypical antipsychotics represent an important therapeutic option for the treatment of bipolar disorder, providing improvements in manic, depressive, and anxiety symptoms.

AN 2004:21458 HCAPLUS <<LOGINID:20080825>>

DN 140:86934

TI The role of atypical antipsychotics in bipolar depression and anxiety disorders

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SO Bipolar Disorders (2003), 5(Suppl. 2), 20-35

CODEN: BDIIAU; ISSN: 1398-5647

PB Blackwell Publishing Ltd.

DT Journal; General Review

LA English

RE.CNT 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2008 ACS ON STN

TI Bipolar depression: Management options

AB A review. Bipolar depression is the predominant abnormal mood state in bipolar disorder. However, despite the key pertinence of this phase of the condition, the focus of research and indeed of clin. interest in the management of bipolar disorder has been mainly on mania. Early studies often failed to distinguish depression due to major unipolar depression from that due to bipolar disorder. Consequently, many treatments used in the management of major depression have been adopted for use in bipolar depression without any robust evidence of efficacy. The selective serotonin reuptake inhibitors (SSRIs), bupropion, tricyclic antidepressants and monoamine oxidase inhibitors are all effective antidepressants in the management of bipolar depression. They are all associated with a small risk of antidepressant-induced mood instability. The mood stabilizers lithium, carbamazepine and valproate semisodium (divalproex sodium) all appear to have modest acute antidepressant properties. Among these, lithium is supported by the strongest data, but the use of lithium in the treatment of bipolar depression as a

monotherapeutic agent is limited by its slow onset of action. Recently, there has been a growing body of evidence suggesting that lamotrigine may have particular effectiveness in both the acute and prophylactic management of bipolar depression. Clin. management of bipolar depression involves various combinations of antidepressants and mood stabilizers and is partly determined by the context in which the depressive episode occurs. In general, "de novo" and "breakthrough" (where the patient is already receiving medication) bipolar depression may be successfully managed by initiating mood stabilizer monotherapy, to which an antidepressant or second mood stabilizer may be added at a later date, if necessary. Breakthrough episodes of bipolar depression occurring in patients receiving combination therapy (two mood stabilizers or a mood stabilizer plus an antidepressant) require either switching of ongoing medications or further augmentation. If this fails, then novel strategies or ECT should be considered. Bipolar depression is a disabling illness and the predominant mood state for the vast majority of those with bipolar disorder. It therefore warrants prompt management once suitably diagnosed, especially as it is associated with a considerable risk of suicide and in the majority of instances is eminently treatable.

AN 2003:66004 HCAPLUS <<LOGINID::20080825>>
 DN 138:147064
 TI Bipolar depression: Management options
 AU Mahi, Gin S.; Mitchell, Philip B.; Salim, Shahzad
 CS School of Psychiatry, University of New South Wales, Sydney, Australia
 SO CNS Drugs (2003), 17(1), 9-25
 CODEN: CNDREF; ISSN: 1172-7047
 PB Adis International Ltd.
 DT Journal; General Review
 LA English
 RE.CNT 174 THERE ARE 174 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2008 ACS ON STN
 TI Depression and dysphoria in adult and adolescent patients with Tourette's disorder treated with risperidone
 AB Depression is a common comorbid condition in patients with Tourette's disorder. While risperidone is not usually known to induce dysphoria or depression in patients treated for other psychiatric disorders, previous short-term 4- to 12-wk trials of risperidone for Tourette's disorder have reported a 2.6% to 30.8% incidence of depression. A retrospective study was carried out in 58 adult and adolescent patients with Tourette's disorder (Tourette Syndrome Classification Study Group diagnosis) who received risperidone between Jan. 1, 1993, and Dec. 31, 2000, at the Allan Memorial Institute, McGill University Health Center, Montreal, Quebec, Canada. Charts of all patients were examined for evidence of, and risk factors for, DSM-IV-defined major depressive disorder (MDD) or dysphoria. Seventeen (29.3%) of 58 patients developed MDD, including 1 patient who later committed suicide and 13 patients (22.4%) who became dysphoric while taking risperidone. Nine of the 17 patients who developed MDD were relapses, i.e., patients with a history of depression prior to taking risperidone, while the remainder were new cases, i.e., patients with no previous history of depression. A pos. personal history of MDD was the only factor to significantly ($p < .001$) predict the development of depression while taking risperidone. Seventy percent of those who developed MDD or dysphoria and discontinued risperidone did so specifically as a result of this adverse event. MDD and dysphoria commonly occurred in this cohort of adult and adolescent Tourette's disorder patients treated with risperidone, particularly in patients with a previous history of depression. Depression and dysphoria were frequent reasons for risperidone discontinuation.

AN 2002:966350 HCAPLUS <<LOGINID::20080825>>
 DN 138:19417
 TI Depression and dysphoria in adult and adolescent patients with Tourette's disorder treated with risperidone
 AU Margolese, Howard C.; Annable, Lawrence; Dion, Yves
 CS Clinical Psychopharmacology Unit, Allan Memorial Institute, McGill University Health Center, Montreal, QC, Can.
 SO Journal of Clinical Psychiatry (2002), 63(11), 1040-1044
 CODEN: JCLPDE; ISSN: 0160-6689
 PB Physicians Postgraduate Press, Inc.
 DT Journal
 LA English
 RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2008 ACS on STN
 TI RNA Editing of the Human Serotonin 5-HT2C Receptor Alterations in Suicide and Implications for Serotonergic Pharmacotherapy
 AB RNA encoding the human serotonin 5-HT2C receptor (5-HT2CR) undergoes adenosine-to-inosine RNA editing events at five positions, resulting in an alteration of amino acids in the second intracellular loop. Several edited 5-HT2CRs possess a reduced G-protein coupling efficiency compared to the completely non-edited isoform. The current studies show that the efficacy of the hallucinogenic drug lysergic acid diethylamide and of antipsychotic drugs is regulated by RNA editing, suggesting that alterations in editing efficiencies or patterns might result in the generation of a 5-HT2CR population differentially responsive to serotonergic drugs. An examination of the efficiencies of RNA editing of the 5-HT2CR in prefrontal cortex of control individuals vs. subjects diagnosed with schizophrenia or major depressive disorder revealed no significant differences in RNA editing among the three populations. However, subjects who had committed suicide (regardless of diagnosis) exhibited a statistically significant elevation of editing at the A-site, which is predicted to change the amino acid sequence in the second intracellular loop of the 5-HT2CR. These findings suggest that alterations in RNA editing may contribute to or complicate therapy in certain psychiatric disorders.
 AN 2001:219717 HCAPLUS <<LOGINID::20080825>>
 DN 135:316832
 TI RNA Editing of the Human Serotonin 5-HT2C Receptor Alterations in Suicide and Implications for Serotonergic Pharmacotherapy
 AU Niswender, C. M.; Herrick-Davis, K.; Dilley, G. E.; Meltzer, H. Y.; Overholser, J. C.; Stockmeier, C. A.; Emeson, R. B.; Sanders-Bush, E.
 CS Department of Pharmacology, Vanderbilt University, Nashville, TN, USA
 SO Neuropsychopharmacology (2001), 24(5), 478-491
 CODEN: NEROEW; ISSN: 0893-133X
 PB Elsevier Science Inc.
 DT Journal
 LA English
 RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT